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Endocrine Functions of the Lungs.

There are two main aims of this research project: the first is to obtain direct evidence on the precise subcellular site of pulmonary angiotensin converting enzyme and to relate these data to understanding of the nonventilatory functions of the lung. The second aim is to develop rapid, simple and sensitive assays of pulmonary angiotensin converting enzyme to facilitate future studies of the effects of physiologic changes and environmental influences (e.g., tobacco smoke) on the ability of the lungs to convert angiotensin I to its potent lower homolog, angiotensin II.

It is now well recognized that the lungs process the circulating vaso-active polypeptides, bradykinin and angiotensin I. Previously, these investigators have postulated that the enzymes responsible for the metabolism of these polypeptides are situated on the luminal surface of pulmonary capillary endothelial cells. Studies from their laboratory over the past six years, as well as from others, have supported the hypothesis but have not proved it. Within the last year, it has been shown that the enzyme that activates angiotensin I (by conversion to angiotensin II) is also responsible for the inactivation of bradykinin. These investigators have raised antibodies to this enzyme, and now propose to use the antibodies labeled for immunocytochemistry to provide a definitive test of their hypothesis.

In addition to testing the hypothesis described above, they would like to undertake a technical program to develop inexpensive, radioactive substrates which will lend themselves to the rapid, simple and sensitive measurement of the turnover rate of angiotensin converting enzyme. Such substrates will be of immediate use in investigations of the ways in which the lungs can modulate their "endocrine" functions in response to physiological stimuli and to inhalants such as tobacco smoke.

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